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(71) Applicant *(for all designated States except US)*: **MARS U.K. LIMITED** [GB/GB]; 3D Dundee Road, Slough SL1 4LG (GB).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **LILLEY, Ian, Andrew** [GB/GB]; 7, Uplands, Birkby, Huddersfield, West Yorkshire HD2 2FS (GB). **MCGENITY, Philip, Martin** [GB/GB]; 17a Green Abbey, Hade Edge, Holmfirth, West Yorkshire HD7 1SH (GB).

(74) Agents: **JACKSON, Richard, Eric** et al.; Carpmaels & Ransford, 43 Bloomsbury Square, London WC1A 2RA (GB).

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(54) Title: FOOD PRODUCT COMPRISING ENCAPSULATED DRUGS

(57) Abstract: The invention relates to food products that contain particles of a pharmaceutical agent dispersed within a palatable food matrix. Each pharmaceutical agent particle is encapsulated within an inert coating. In this manner, the unpleasant taste of the pharmaceutical agent is disguised, and the pharmaceutical agent is not susceptible to modification or degradation as a result of contacting compounds contained within the food matrix.

FOOD PRODUCT COMPRISING ENCAPSULATED DRUGS

The present invention relates to food products that contain a pharmaceutical agent dispersed within a palatable food matrix. The products are designed so that the unpleasant taste of the pharmaceutical agent is disguised. Additionally, the pharmaceutical agent is not susceptible to modification or degradation as a result of contacting compounds contained within the food matrix. This guarantees the safety of the product.

The maintenance of good health and the treatment of ill health in animals, especially companion animals, is frequently achieved by the oral administration of medications and supplements. Examples include the treatment or prevention of worms and fleas, the treatment of a range of infections and the treatment of arthritic symptoms and other ailments typical of older animals.

Typically, one or more pharmaceutical agents are dispersed within a matrix of substantially inert materials and formed into a tablet or lozenge. Inert materials are used to prevent reaction of the pharmaceutical agent with compounds contained within the food.

These inert materials are generally selected from a range of such materials that are specified in approved Pharmaceutical monographs, such as the European Pharmacopoeia. Such collections of monographs tend to exclude many of the materials which are most palatable to many animals, such as meat products and complex proteins, at least partly because their complexity makes it almost impossible to define a very precise specification for such materials. This makes it difficult to design medicinal food products that are palatable to the animal.

Palatability is of great significance, particularly for fastidious companion animals such as cats, since oral administration of an unpalatable tablet can be very difficult and on occasions even impossible, particularly when the agents to be administered are especially unpalatable to the animal.

Palatability is also important when baiting wild animals, for example, for the delivery of vaccines or other pharmaceutical formulations. In this instance, it is of the utmost importance to ensure that the active agents are successfully ingested by the wild animal, since it will be desirable for as many animals as possible to receive the intended treatment.

The problem of the oral administration of unpalatable medicine to animals has been recognised in the art, and a number of solutions have been proposed.

One approach is to create a product, using pharmaceutical agents that are relatively stable chemically, that consists of one or more pharmaceutical agents dispersed within a palatable matrix of pet food materials. Analytical methods are then employed to validate that, within the resolution of such methods, the pharmaceutical agents are not degraded, either during processing, or simply through being in contact with food materials. Such a product, known as "Esy-Dose", is currently sold in Australia.

However, this approach has some drawbacks. Firstly, the approach will not be successful with pharmaceutical agents that are not stable in the presence of food materials. Secondly, even though analytical methods may show, within their resolution, that no degradation of the pharmaceutical agent nor any interaction of the agent with the food matrix has occurred, there is always a concern that such degradation or interaction of the pharmaceutical may in fact have occurred, but to an extent too slight to be resolved by the analytical methods available.

A related concern is that the complexity and variability of materials such as meat products, that could well be present in such a palatable matrix, may be such that the occasional batch of such a material might be exceptionally more chemically reactive towards the pharmaceutical agent. Because this event is only very occasional, this possibility may not be apparent during the validation procedures.

Such concerns have led the pharmaceutical regulatory authorities in some countries to err on the side of caution, and to indicate an unwillingness to grant licenses to companies to sell products of this type.

EP 0 574 301 (Sogeval SA) teaches an alternative solution, namely that of using a matrix of palatable food material which contains a "recess" within which a pill can be placed. A similar principle is described in International patent application WO95/20942 (Atali & Vuagnoux). Experience shows, however, that many animals are quite capable of "sifting out" the less palatable pill from the more palatable matrix, thus leaving the medication substantially untouched.

Another approach is to disperse the pharmaceutical active within a core and to apply an outer coating layer, which includes palatable substances, as is described in US 5,683,722 (Derrieu *et al.*). However, experience again shows that many animals are capable of consuming palatable coatings (for example, by licking), leaving the less palatable core untouched.

A variation on this theme is to affix particles of a pharmaceutical agent to a core particle of food material, as described in US 5,624,710 (Dox-AL Italia SpA). This solution is intended to facilitate subsequent distribution within a feed. However, this approach suffers from the drawback that there is no barrier between the pharmaceutical agent and the food, with the negative consequences outlined above.

Yet another approach is to disperse the active in an inert matrix of materials taken from a relatively restricted range of those which have pharmacopoeia monographs and to create a granule, which may then be added to a feed. Such an approach is taught in US 4,597,969 (Merck, Sharp & Dohme), where the granule is formed from alginates and magnesium hydroxide. However, the ability of many animals to "sift out" particles of unpalatable material from others which are more palatable presents a significant drawback to this approach.

There thus remains a great need for a system to deliver reliably a pharmaceutical agent to an animal. Such a system would allow incorporation of the agent into food products without compromising the palatability of the food, whilst ensuring that no unwanted chemical reactions take place between the food ingredients and the pharmaceutical.

Summary of the invention

According to the invention, there is provided a food product for the oral delivery of a pharmaceutical agent to a non-human animal, comprising particles of said agent dispersed substantially uniformly within a palatable food matrix, wherein each of said particles is encapsulated within a substantially inert coating.

The food products of the invention have the advantage that they greatly increase the ease and chance of success of oral administration, by suppressing the unpalatable taste of the medicament, whilst minimising the risks associated with bringing pharmaceutical agents directly into contact with food components. The pharmaceutical agent is isolated from the

food material by virtue of the inert coating surrounding the agent, meaning that no undesirable reactions can occur between the pharmaceutical agent and the other ingredients of the food product. This greatly increases the range of pharmaceutical agents that may be included in food products. Furthermore, a large selection of food ingredients may be used to ensure that the product exhibits the desired degree of palatability to the target animal, since the selection is not limited to the substantially inert materials that are generally approved for contact with pharmaceutical agents.

A further advantage of the food products of the invention is that they provide an excellent mechanism by which to control the dosage of medicament that is applied to the animal. A certain product type, designed for a particular application to a specific target animal, will therefore contain a controlled amount of medicament. This amount should correspond to the desired dosage for a particular unit weight of animal, for example, a 10kg unit weight. The owner or carer of the animal can in this way administer the required dosage simply by reference to the weight of the animal. In this example, a 30kg animal would be given three food products.

The food products of the invention may be liquid, semi-solid or solid in form. Solid food products may be formed into lozenges or tablets that contain a particular unit dose of pharmaceutical agent. Strips or chews may also be used. Semi-solid products may take the form of a porridge or broth. Liquid food products may be packaged into cans or tins, preferably in amounts corresponding to a particular unit dose.

The food matrix may be any material that is palatable, non-toxic, and easily ingestable, including solid, semi-solid and liquid materials. Preferably, the matrix is easily digestible by the animal. Suitable food materials may be selected from those used conventionally in pet foods and livestock feed, as the skilled reader will appreciate. Typically, the matrix will contain flours and starches and other materials necessary to aid processing, impart colour, act as preservatives, impart texture and so on.

A selection of typical ingredients is given below, with the function of each ingredient given in parentheses: poultry meal (protein source, palitant); soya bean oil (fat, aid to processing); poultry liver powder (protein, palitant); sugar (flavour, humectant); glycerol (softener, humectant); water (texture former, aid to processing); maltose glucose syrup (flavour, humectant); salt (flavour, humectant); dark malt flour (starch, colorant); red iron

oxide (mineral); burnt sugar (flavour); pre-gel waxy maize starch (starch, texture former); turkey flavour (flavour, palitant); roche D20 (antioxidant).

For administration to carnivorous companion animals such as dogs and cats, meat and fish-based materials may also be used in the food matrix. These materials are generally derived from dried meat and fish products that are then formed into powders for incorporation into food materials.

Milk is particularly suitable as a food matrix for a liquid food product, since it is highly palatable, allows homogenous dispersion of the encapsulated particles of pharmaceutical agent and may be easily packaged and stored without risk of degradation.

The products may optionally be divided into fractions to allow precise administration of the correct dose to an animal that falls between two weight groupings. For example, a product in the form of a lozenge, tablet, strip or chew may be marked into segments (for example, into quarters).

The products of the invention may be administered directly to the animal, for example, by hand. Alternatively, the products may be mixed into the animal's food. For ease of ingestion, solid food products such as lozenges or tablets may be broken into small portions, once the correct number of units has been measured out.

A large range of pharmaceutical agents may be included in the food products of the invention, as will be clear to the skilled reader. After an animal has been formally diagnosed by a veterinary surgeon as suffering from a particular disease or condition, a course of medicaments may be prescribed. Particular examples include agents to treat or prevent parasite infestation, such as anti-worming agents, agents directed against stiffness or arthritis, components of vaccines, anti-flatulence agents, antibiotics, agents for the treatment of obesity, agents for the treatment of motor disorders, agents for the treatment of senility, agents for the treatment of elevated blood pressure, anti-inflammatory agents, oral rehydration agents, hormones, diuretics, cardiovascular and respiratory preparations, products to thin the blood or enhance circulation and agents directed against unpleasant breath odour. Other examples will be quite clear to the skilled reader and many are listed in appropriate reference works such as the National Office of Animal Health compendium of data sheets for veterinary products.

For many conditions, such as, for example, worm infections the carer or owner of the animal may be able to diagnose a suitable treatment without needing to consult a vet. The food products of the invention may thus be available over the counter in stores such as supermarkets and pet shops.

For application to companion animals such as dogs, cats, rabbits and the like, particularly suitable examples of pharmaceutical agents include anti-worming compounds such as dichlorophen, febantel, fenbendazole, mebendazole, nitroscannate, piperazine, praziquantel, pyrantel, and oxantel. Medicament may also be applied to livestock, such as horses, cattle, sheep, pigs and goats. Examples of suitable agents include albendazole and oxfendazole.

Of course, in cases where the pharmaceutical agents are compatible with one other, the agents may be combined into one product type to give a combined medicament. In cases where pharmaceutical agents would react undesirably with one another if brought into contact, each agent may be individually encapsulated and mixed into the food matrix separately. In a further embodiment, individually encapsulated pharmaceutical agents may be agglomerated into combined particles and further encapsulated.

It is also intended that wild animals susceptible to disease may be treated using bait laced with the food products of the invention. In this manner, a vaccine such as, for example, an anti-rabies vaccine, may be administered to wild animals such as foxes. Animals such as deer may be treated with anti-tick vaccines. Other examples will be apparent to those of skill in the art and will vary throughout the countries of the world. In certain circumstances, poisons may also be delivered using the food products of the invention, for example, to limit a pest population.

The pharmaceutical agent should be dispersed throughout the food matrix as small encapsulated particles. The size of these particles may vary between certain limits, depending on various factors such as the nature of the medicament, the method of processing, the target animal species, the cost of production and the intended sales value of the food products. The particle size should be small enough that the integrity of the encapsulated pharmaceutical is retained through the manufacturing process; if the particles are too large, there is a risk that during mixing of the particles within the food matrix, the particles will become broken by shearing forces. Furthermore, a large particle size

increases the chance that the particles may become broken during chewing of the food by the animal, meaning that the unpalatable pharmaceutical agent will be tasted and the food rejected.

However, there is no need to generate very minute particles and indeed, the expense involved in the production of extremely small particles is significant. Generally, the particles will be between 100nm and 1mm in diameter, preferably between 1 and 500μm diameter, more preferably between 150 and 500μm diameter.

The thickness of the encapsulating coating may also be varied, depending on the particular requirements of each system. The coating must be sufficiently mechanically robust to withstand the high shearing forces encountered during the production and molding process, but must not be so thick that the particles pass through the digestive system without being ingested. An additional factor is that as more coating material is used in the production process, the cost of materials increases. Ideally, the coating should be thick enough to prevent it degrading until the food has passed out of the buccal cavity into the lower regions of the oesophagus, where the palatability of the food is no longer of concern. A preferred range for the thickness of the coating is between 1nm and 100μm, more preferably, between 20nm and 100nm. The ratios of coating to core may vary between around 1:20, to around 1:1, depending upon the particular requirements and properties desired of the food product.

The use of encapsulation is very widespread, particularly in the pharmaceutical industry (see, for example, Saeki and Hosoi (1984) Biochemistry and Biotechnology 10:251; Tirkkonen *et al.*, (1994) J. Microencapsulation 11(6), 615-626; Takeda *et al.*, (1981) 29(1), 264; Palmieri *et al.*, (1992) Drug development and industrial pharmacy 22(9& 10), 951; Meyer (1992), Chimia 46, 101; Koida *et al.*, (1983) Chem. Pharm. Bull. 31(12), 4476; Jalsenjak *et al.*, (1976) J. Pharm. Pharmac., 28, 912; Tirkkonen and Paronen (1993) Int. J. Pharmaceutics 92: 55; Al-Musa *et al.*, (1999) 57: 223). Often, the purpose is to control the release of a pharmaceutical agent after administration, so that, for example, it is released in a particular part of the digestive system or it is released gradually over time so that the duration of its effect is extended. Encapsulation has also been used in both pharmaceuticals and flavour compounds to help to protect from losses during processing.

The encapsulating coating should be made or derived from substantially inert materials specified by a monograph in a recognised pharmacopoeia, such as the European Pharmacopoeia. Other suitable encapsulating agents will be known to those of skill in the art. Examples of inert encapsulating materials include ethylcellulose, gelatine and gum arabic. By "substantially inert" is meant that the material is non-reactive chemically under conditions of normal temperature and pressure with food matrix materials and with pharmaceutical agents. The encapsulating coating should not itself be a recognised pharmaceutical agent and should be safe to eat.

Any method of generation and encapsulation of small particles will be suitable for use in the present invention, as the skilled reader will appreciate. In general, there are three main methods by which encapsulated particles may be most easily generated.

For pharmaceutical agents that are soluble in organic solvents, and that are insoluble in water, a co-assivation technique may be applied. A particulate suspension of the agent is prepared, for example, in a solution of ethylcellulose in cyclohexane. This solution is then stirred vigorously. The particles will in this manner gradually become encased within an ethylcellulose coating. The size of the particles can be controlled by the speed of stirring the solution; faster stirring will result in a smaller particle size. The thickness of the coating may be controlled by altering the amount of encapsulating agent that is present in the solvent. A larger amount of encapsulating agent will increase the thickness of the coating layer.

A second method, also suitable for use with water-insoluble pharmaceutical agents, involves spraying a solution of the pharmaceutical agent into a bath of calcium chloride. The pharmaceutical agent may be dissolved in a sodium alginate solution and then sprayed into the bath, thus creating an atomised aerosol that forms encapsulated particles. The force with which the liquid is sprayed controls the particle size; the faster spraying is operated, the smaller will be the resulting particle size. Again, the thickness of the coating can be controlled by varying the content of encapsulating material.

A third method utilises co-assivation of a gelatine/gum arabic mixture in an aqueous solution, within which the pharmaceutical agent is dispersed. The suspension is stirred until the particles reach the desired size, then the pH is adjusted, forcing the gelatine/gum arabic mixture back out of solution to form deposits on the surface of each particle. The

thickness of the encapsulated layer can be controlled by varying the content of the gelatine/gum arabic material.

Once the particles of encapsulated pharmaceutical have been prepared, they are mixed into the food matrix to form a homogenous mixture, in which the particles are mixed substantially uniformly. By "substantially uniformly" is meant that the particles are dispersed throughout the food matrix and do not agglomerate together in lumps. To ensure that a substantially uniform dispersion is created, the food matrix must be mixed with the particles for a sufficient time. As the skilled reader will appreciate, the mixing period will differ for different particle sizes and for different food matrix materials. If necessary, samples can be taken at time points during the mixing process and analysed to assess the degree to which mixing has occurred. The most effective way to ensure that complete mixing has occurred is to blend the mixture for an extended period of time.

In the case of solid products, the mixture of food matrix and encapsulated pharmaceutical particles that results at the end of the mixing process may then be molded into the desired shape. These products may be any shape, but will normally be spherical, square, rectangular, cylindrical or pill-shaped. However, to increase their consumer appeal, the products may be formed into attractive shapes such as, for example, the shape of a bone. As discussed above, molded products may include indentations that mark out fractions of the product, so allowing the product to be broken into segments to facilitate the correct dosing. Finally, the products will be packaged for sale. Packages that contain one or more food products as described above are included as part of the present invention.

According to a further aspect of the invention, there is provided a process for the production of a food product containing a pharmaceutical agent suitable for administration to a non-human animal, comprising the step of dispersing particles of said agent substantially uniformly within a palatable food matrix, wherein each of said particles is encapsulated within a substantially inert coating.

According to a still further aspect of the invention, there is provided a food product according to any one of the above-described aspects of the invention, for use in therapy of a non-human animal. The invention also provides the use of particles of a pharmaceutical agent encapsulated within a substantially inert coating and dispersed within a palatable

food matrix, in the manufacture of a medicament for the treatment or prevention of a disease in a non-human animal.

A still further aspect of the invention provides a method of treating a disease, or of preventing incidence of a disease in a non-human animal, comprising administering to said animal, a food product according to any one of the aspects of the invention described above.

Various aspects and embodiments of the invention will now be described in more detail by way of example, with particular reference to fenbendazole and praziquantel as pharmaceutical agents. It will be appreciated that modification of detail may be made without departing from the scope of the invention.

Examples

Example 1 : Encapsulation of Fenbendazole in Calcium Alginate

Sodium Alginate (40.0 g) was dissolved in hot water (2 kg) with vigorous stirring. Fenbendazole (100 g) was added and the resulting suspension homogenised using a high shear Silverson mixer, before dilution with water (1 Kg).

Calcium chloride (45.0 g) was dissolved in water (3 Kg) and agitated in a large diameter bowl. The fenbendazole-alginate suspension was sprayed into the calcium chloride solution, setting the alginate, and generating a slurry of fenbendazole entrained in alginate gel. The slurry was filtered, oven dried, then graded through 'Endecott' precision sieves to give the encapsulated Fenbendazole with a particle size predominately in the range 150-500 µm which was analysed for free fenbendazole according to the standard test conditions.

Particle Size	Free Fenbendazole	Total Fenbendazole Content
150µm	16.6%	52.9%
250µm	10.6%	66.2%
500µm	6.2%	76.9%

Example 2 : Encapsulation of Fenbendazole in Gelatine – Acacia

Gelatine (10 g) and acacia (10 g) were dissolved separately in water at 40°C. Fenbendazole (20 g) was added to the gelatine solution and the resulting suspension homogenised using a high shear Silverson mixer. The acacia solution was added, the suspension re-homogenised and then diluted to a concentration of 1.5% (w/v) based on the individual colloids. The pH of the suspension was adjusted to 4.5 over 1 hour by the addition of 10% acetic acid in water, held for 1 hour at 40°C then cooled to 15°C over 2 hours. The solution was diluted with isopropanol (200 ml), filtered then dried to give free flowing particles. These were graded through 'Endecott' precision sieves to give the encapsulated Fenbendazole with a particle size predominately in the range 150-500 µm, which was analysed for free fenbendazole according to the standard test conditions.

Particle Size	Free Fenbendazole	Total Fenbendazole Content
250µm	4.6%	43%

Example 3 : Encapsulation of Praziquantel in Calcium Alginate

Sodium Alginate (8.4 g) was dissolved in hot water (700 g) with vigorous stirring. Praziquantel (5.2 g) was added and the resulting suspension homogenised using a high shear Silverson mixer. Calcium chloride (11.2 g) was dissolved in water (800 g) and agitated in a large diameter bowl. The praziquantel-alginate suspension was sprayed into the calcium chloride solution, setting the alginate, and generating a slurry of praziquantel entrained in alginate gel. The slurry was filtered and the resultant high moisture content solid analysed for free Praziquantel according to the standard test conditions.

Analytical Procedure for Determination of Free Fenbendazole and Praziquantel

Methanol – DMSO (9:1) was demonstrated as a suitable solvent for the free active while having the potential to leave the encapsulating materials intact over a short time period (Based on data obtained from The Merck Index (11th Edition), Merck and Co, 1989). The sample was diluted with solvent in a 50 ml volumetric flask, shaken for 2 minutes to dissolve free active then sample. The sample was analysed by HPLC against an external

standard (C18 column, eluant 70 : 30 MeOH : H_2O, flow rate 1.5ml.min, detection at 290 nm) to give a T_0 value for free active. The solution was samples over the course of 2 hours to give an indication of the degradation rate of the wall and the leach rate from the capsule. In order to determine the total active content of the capsules, the capsules were ground with methanol – DMSO (9:1) in order to mechanically disrupt the capsule walls, sonicated for 15 minutes to ensure full dissolution of the released active, then analysed by HPLC.

Time (mins)	150µm	250µm	500µum
0	16.6%	10.6%	6.2%
10	19.5%	12.4%	8.1%
30	22.5%	14.8%	10.3%
60	24.6%	16.5%	11.3%
120	25.1%	16.8%	11.7%
Total Fenbendazole Content	52.9%	66.2%	76.9%

Example 4: Microencapsulation to Enhance Palatability.

Praziquantel was encapsulated in calcium gelled alginate as previously described. The resultant colourless powder was dispersed in a powder premix and the bonding agent added. The resultant dough was maintained at 60°C in order to keep it workable, while being formed into 2.5g treats.

Recipe

Powder Premix

Ingredient	Weight/g	Percentage	**Ingredient**	Weight/g	Percentage
Powdered Cat Treat	73.7	53.80%	Antioxidant	0.49	0.36%
Fish Flour	24.6	17.96%	Amino acids	0.6	0.44%
Cereal Flour	5.9	4.31%	Xylose	0.34	0.25%
Salt	4.18	3.05%	Encapsulated Praziquantel	2.2	1.61%
Potassium Sorbate	0.25	0.18%			

Bonding Agent

Ingredient	Weight/g	Percentage
Cat Baste	4.03	2.94%
Glycol	4.03	2.94%
Gelatine	2.48	1.81%
Palitant	4.19	3.06%
Water	10.0	7.30%

Feeding Trials

The product was fed to cats in three separate trials and acceptance of the product compared against a control product. The final trial tested whether aversion to the treat was introduced when the product was repeat fed. As a control, a feeding trial was carried out using non-encapsulated material. The results are summarised below.

Although sample sizes are in all cases small (15 cats), the results indicate that a significant enhancement in palatability can be achieved through the use of encapsulation. The percentage values given represent the percentage of cats which either accepted the product when offered from the hand, or which accepted the product when scattered onto food.

A slight deterioration in performance is observed after feeding the treat on successive days, however the feeding pattern for worming treats is a once a month occasion. A further improvement in performance can be expected through an improvement in the palatability of the base recipe.

	Control	**Wormer : 1st Occasion**	**Wormer : 2nd Occasion**
Trial One (non-encapsulated)	75%*	25%	-
Trial Two (encapsulated)	60%	40%	-
Trial Three (encapsulated)	62%	46%	-
Trial Four (encapsulated)	60%	75%	60%

* = placebo used was "Thomas's seafood for cats"

Example 5: Microencapsulation to Enhance Stability.

An oral insecticide was encapsulated in ethyl cellulose, as previously described. The

resultant colourless powder was then dispersed in a powder premix and subjected either to a standard thermal process (T=120°C) or to a mild process (T=45°C). The resultant treats were analysed for active content and compared with the expected value.

Standard Process Recipe

Ingredient	%	Ingredient	%
Cereal Flour	15.59	Sugars	11.03
Dried Meat/Fish	44.03	Glycerol	7.55
Gluten	1.88	Sunflower Oil	7.55
Salt	1.88	Cat Baste	3.36
Amino Acids	0.43	Whitings	2.88
Antioxidant	0.21	Insecticide	1.92
		Palitant	1.68

Baked at 120°C for 20 minutes

Mild Process Recipe

Step One : Prepare placebo recipe:

Ingredient	%	Ingredient	%
Cereal Flour	16.22	Sugars	11.48
Dried Meat/Fish	45.81	Glycerol	7.85
Gluten	1.96	Sunflower Oil	7.85
Salt	1.96	Cat Baste	3.5
Amino Acids	0.44	Whitings	5.0
Antioxidants	0.22	Palitant	1.75

Moulded to give treats of 5.5g per piece, then baked at 120°C for 19 minutes.

Step Two : Preparation of Bonding Agent

Ingredient	Percentage	Ingredient	Percentage
Water	43.75%	Glycerol	16.25%
Gelatin	25%	Potassium Sorbate	1%
Sucrose	14%		

Gelatin was added to boiling water, stirred to dissolve, then sucrose added. On dissolution of the sucrose, glycerol was added followed by potassium sorbate, and the solution homogenised. The resultant solution was then allowed to cool to solidify.

Step 3 : Preparation of Mild Process Treat

Powdered placebo (874.7g) and Oral Insecticide (20.0g) were mixed thoroughly to ensure complete homogeneity. Solid bonding agent (105.2g) was cut into small (~5mm^3) cubes, added to the powder premix and mixed thoroughly. The raw material was then heated to 40°C in a stirred mixer to give workable dough that was moulded by hand.

Recovery Results

Sample	Unencapsulated	Encapsulated
Baked	56.6%	66.5%
Mild process	95.9%	~100%

An increase in stability through the thermal process can be observed through the use of encapsulation.

CLAIMS

1. A food product for the oral delivery of a pharmaceutical agent to a non-human animal comprising particles of said agent dispersed substantially uniformly within a palatable food matrix, wherein each of said particles is encapsulated within a substantially inert coating.

2. A food product according to claim 1, wherein said pharmaceutical agent is an anti-parasitic agent, an agent with efficacy against stiffness or arthritis, a component of a vaccine, an anti-flatulence agent, or an agent effective against unpleasant breath odour.

3. A food product according to claim 2, wherein said anti-parasitic agent is an anti-worming agent.

4. A food product according to any one of the preceding claims, wherein said encapsulated particles are between 1nm and 1mm in diameter.

5. A food product according to claim 4, wherein said encapsulated particles are between 20nm and 100μm in diameter.

6. A food product according to any one of the preceding claims, which is formed as a tablet, lozenge, strip or chew.

7. A food product according to claim 6, wherein said product is molded.

8. A food product according to any one of claims 1-5, wherein said food matrix comprises liquid milk.

9. A food product according to any one of the preceding claims, wherein said palatable food matrix comprises a meat or fish derivative.

10. A food product according to any one of the preceding claims, wherein said inert coating comprises ethylcellulose, gelatine or gum arabica.

11. A food product according to any one of the preceding claims, wherein the amount of said pharmaceutical agent in the product corresponds to a recommended unit dose for a unit of animal bodyweight.

12. A food product according to claim 11, wherein said unit of animal bodyweight is a 10kg unit.

13. A food product according to any one of the preceding claims, wherein said product is divided into defined segments.

14. A package comprising one or more food products according to any one of the preceding claims.

15. A process for the production of a food product containing a pharmaceutical agent suitable for administration to a non-human animal, comprising the step of dispersing particles of said agent substantially uniformly within a palatable food matrix, wherein each of said particles is encapsulated within a substantially inert coating.

16. A food product according to any one of claims 1-13, for use in therapy of a non-human animal.

17. Use of particles of a pharmaceutical agent encapsulated within a substantially inert coating in the manufacture of a medicament for the treatment or prevention of a disease in a non-human animal, wherein said particles are dispersed within a palatable food matrix.

18. Use according to claim 17, wherein said disease is a parasitic infection, arthritis or stiffness.

19. A method of treating a disease, or of preventing the incidence of a disease in a non-human animal, comprising administering to said animal, a food product according to any one of claims 1-13.

INTERNATIONAL SEARCH REPORT

Int tional Application No
PCT/GB 00/04405

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K9/00 A61K9/20

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
WPI Data, PAJ, EPO-Internal, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 18610 A (VAN LENGERICH, BERNHARD) 7 May 1998 (1998-05-07) figures 1-5 claims 1,4-6,20 page 21, line 20 - line 30 page 35, line 1 - line 13 ---	1-19
A	LU, BIN; ET AL.: "Preparative studies on praziquantel microcapsules" ZHONGGUO YIYAO GONGYE ZAZHI BIANJIBU, vol. 28, no. 4, 1997, pages 159-161, XP000986678 CN abstract --- -/--	1-19

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
22 February 2001	05/03/2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx 31 651 epo nl, Fax: (+31-70) 340-3016	Ventura Amat, A

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INTERNATIONAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Q. A. MCKELLAR; ET AL: "Pharmacokinetics of fenbendazole in dogs" JOURNAL OF VETERINARY PHARMACOLOGY AND THERAPEUTICS, vol. 13, no. 4, 1990, pages 386-392, XP000986683 the whole document	1-19

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INTERNATIONAL SEARCH REPORT

Int tional Application No
PCT/GB 00/04405

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9818610 A	07-05-1998	AU 4991597 A	22-05-1998
		EP 0935523 A	18-08-1999
		NO 992036 A	28-04-1999
		PL 333095 A	08-11-1999